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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JUL 20	Powerful new interactive analysis and visualization software, STN AnaVist, now available
NEWS	4	AUG 11	STN AnaVist workshops to be held in North America
NEWS	5	AUG 30	CA/CAplus -Increased access to 19th century research documents
NEWS	6	AUG 30	CASREACT - Enhanced with displayable reaction conditions
NEWS	7	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS	8	SEP 22	MATHDI to be removed from STN

NEWS EXPRESS	JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:28:23 ON 30 SEP 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:28:27 ON 30 SEP 2005
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Property values tagged with IC are from the ZIC/VINITI data file

provided by InfoChem.

STRUCTURE FILE UPDATES: 28 SEP 2005 HIGHEST RN 864132-17-2
DICTIONARY FILE UPDATES: 28 SEP 2005 HIGHEST RN 864132-17-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

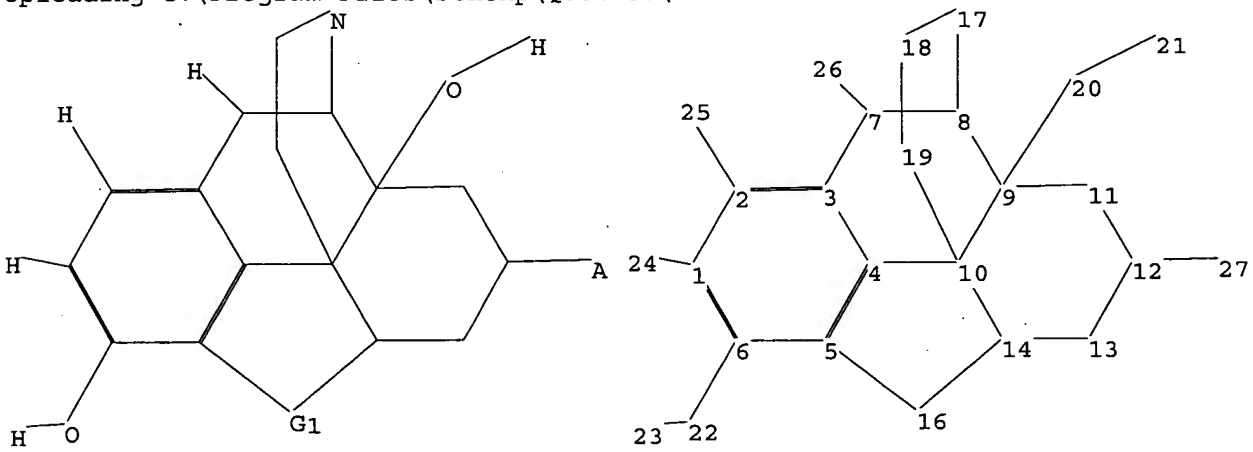
Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\333.str



chain nodes :
20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 16 17 18 19
chain bonds :
1-24 2-25 6-22 7-26 9-20 12-27 20-21 22-23
ring bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-10 5-6 5-16 7-8 8-9 8-17 9-10 9-11 10-14
10-19 11-12 12-13 13-14 14-16 17-18 18-19
exact/norm bonds :
1-24 2-25 3-7 4-10 5-16 6-22 7-8 7-26 8-9 8-17 9-10 9-11 9-20 10-14
10-19 11-12 12-13 12-27 13-14 14-16 17-18 18-19 20-21 22-23

normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

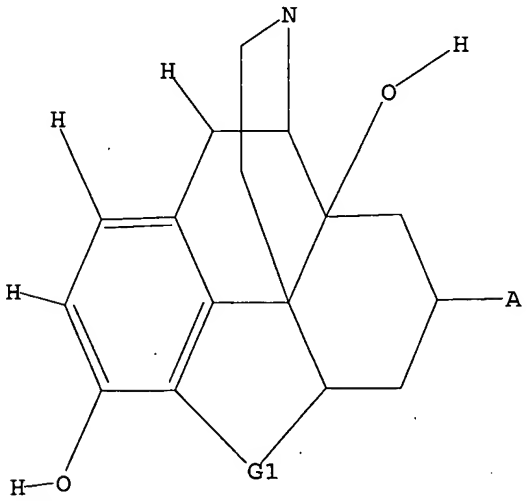
G1:O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

L1 STRUCTURE UPLOADED

=> ed l1
ED IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sam
SAMPLE SEARCH INITIATED 09:28:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 498 TO ITERATE

100.0% PROCESSED 498 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8622 TO 11298

10/665377

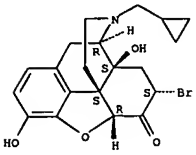
PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

=> d scan

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinan-6-one,
7-bromo-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-,
(5α,7α)- (9CI)
MF C20 H22 Br N O4
CI COM

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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=> s l1 full
FULL SEARCH INITIATED 09:28:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      9392 TO ITERATE

100.0% PROCESSED      9392 ITERATIONS                                  77 ANSWERS
SEARCH TIME: 00.00.01

L3            77 SEA SSS FUL L1

=> file ca
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     161.33     161.54

FILE 'CA' ENTERED AT 09:28:55 ON 30 SEP 2005
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COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 29 Sep 2005 VOL 143 ISS 15
FILE LAST UPDATED: 29 Sep 2005  (20050929/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4            10 L3

=> d ibib abs fhitstr
```

L4 ANSWER 1 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:179658 CA
TITLE: Opioid tannate compositions
INVENTOR(S): Chopdekar, Vilas M.; Redkar, Sham N.; Schlek, James R.
PATENT ASSIGNEE(S): Jame Fine Chemicals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S. Provisional Ser. No. 446,230.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

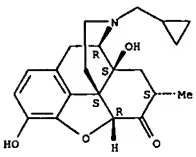
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004157784	A1	20040812	US 2003-734460		20031212
PRIORITY APPLN. INFO.:			US 2003-446230P	P	20030210

AB Compns. comprise the tannates of opioids. The opioid tannate may be readily prepared by reacting an opioid free base such as hydrocodone or oxycodone with tannic acid, either neat or in the presence of up to about 30 weight % water, at a temperature of about 60 to about 150° C. and thereafter recovering the resultant opioid tannate. The opioid tannate may also be prepared by an alternative process that involves reacting the opioid free base with water at a temperature such that not more than about 10 weight % of the opioid tannate will be decomposed and thereafter removing the water by freeze-drying.

IT 79413-55-1DP, tannate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opioid tannate compns.)

RN 79413-55-1 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-methyl-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 1 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)

=> d ibib abs fhitstr all

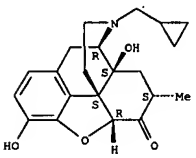
L4 ANSWER 1 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:179658 CA
TITLE: Opioid tannate compositions
INVENTOR(S): Chopdekar, Vilas M.; Redkar, Sham N.; Schlek, James R.
PATENT ASSIGNEE(S): Jame Fine Chemicals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S. Provisional Ser. No. 446,230.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004157784	A1	20040812	US 2003-734460	20031212
PRIORITY APPLN. INFO.:			US 2003-446230P P	20030210

AB Compns. comprise the tannates of opioids. The opioid tannate may be readily prepared by reacting an opioid free base such as hydrocodone or oxycodone with tannic acid, either neat or in the presence of up to about 30 weight % water, at a temperature of about 60 to about 150° C. and thereafter recovering the resultant opioid tannate. The opioid tannate may also be prepared by an alternative process that involves reacting the opioid free base with water at a temperature such that not more than about 10 weight % of the opioid tannate will be decomposed and thereafter removing the water by freeze-drying.

IT 79413-55-1DP, tannate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opioid tannate compns.)
RN 79413-55-1 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-methyl-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 141:179658 CA
ED Entered STN: 02 Sep 2004

L4 ANSWER 1 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)
IT 50-36-2DP, Cocaine, tannate 57-27-2DP, Morphine, tannate, biological studies 57-42-1DP, Meperidine, tannate 76-41-5DP, Oxymorphone, tannate
76-57-3DP, Codeine, tannate 76-99-3DP, Methadone, tannate 77-07-6DP, Levorphanol, tannate 125-28-0DP, Dihydrocodeine, tannate 125-29-1DP, Hydrocodone, tannate 359-83-1DP, Pentazocine, tannate 437-38-7DP, Fentanyl, tannate 465-65-6DP, Naloxone, tannate 466-99-9DP, Hydromorphone, tannate 469-62-5DP, Propoxyphene, tannate 509-60-4DP, Dihydromorphine, tannate 561-27-3DP, Diacetylmorphine, tannate 915-30-0DP, Diphenoxylate, tannate 1477-40-3DP, Levo-α-acetylmethadol, tannate 14357-78-9DP, Diprenorphine, tannate 14521-96-1DP, Etorphine, tannate 16590-41-3DP, Naltrexone, tannate 20594-83-6DP, Nalbuphine, tannate 27203-92-5DP, Tramadol, tannate 42408-82-2DP, Butorphanol, tannate 51931-66-9DP, Tilidine, tannate 52485-79-7DP, Buprenorphine, tannate 53648-55-8DP, Dezocine, tannate 55096-26-9DP, Nalmefene, tannate 56030-54-7DP, Sufentanil, tannate 59708-52-0DP, Carfentanil, tannate 61380-40-3DP, Lofentanil, tannate 71195-58-9DP, Alfentanil, tannate 79413-55-1DP, tannate 132875-61-7DP, Remifentanil, tannate 736142-24-8DP, tannate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opioid tannate compns.)

L4 ANSWER 1 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)
TI Opioid tannate compositions
IN Chopdekar, Vilas M.; Redkar, Sham N.; Schlek, James R.
PA Jame Fine Chemicals, Inc., USA
SO U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S. Provisional Ser. No. 446,230.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-70
ICS A61K031-522; A61K031-60; A61K031-485; A61K031-46
INCL 514023000; 514165000; 514263320; 514282000; 514304000
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004157784	A1	20040812	US 2003-734460	20031212
PRAI US 2003-446230P	P	20030210		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004157784	ICM	A61K031-70
	ICS	A61K031-522; A61K031-60; A61K031-485; A61K031-46
	INCL	514023000; 514165000; 514263320; 514282000; 514304000
US 2004157784	NCL	514/023.000
	ECLA	A61K031/46; A61K031/485; A61K031/522; A61K031/60; A61K031/70

AB Compns. comprise the tannates of opioids. The opioid tannate may be readily prepared by reacting an opioid free base such as hydrocodone or oxycodone with tannic acid, either neat or in the presence of up to about 30 weight % water, at a temperature of about 60 to about 150° C. and thereafter recovering the resultant opioid tannate. The opioid tannate may also be prepared by an alternative process that involves reacting the opioid free base with water at a temperature such that not more than about 10 weight % of the opioid tannate will be decomposed and thereafter removing the water by freeze-drying.

ST opioid tannate prepn
IT Tannins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opioid salts)
IT Freeze drying
Particle size
(opioid salts with)
IT Opioids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid tannate compns.)
IT 143-71-5, Hydrocodone bitartrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(opioid tannate compns.)
IT 125-29-1P, Hydrocodone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(opioid tannate compns.)

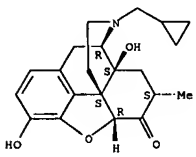
=> d ibib abs fhitstr 1-10

L4 ANSWER 1 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:179658 CA
TITLE: Opioid tannate compositions
INVENTOR(S): Chopdekar, Vilas M.; Redkar, Sham N.; Schlek, James R.
PATENT ASSIGNEE(S): Jame Fine Chemicals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S. Provisional Ser. No. 446,230.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

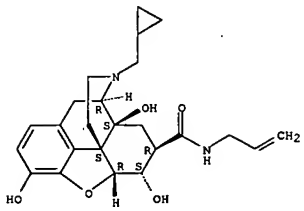
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004157784	A1	20040812	US 2003-734460	20031212
PRIORITY APPLN. INFO.:			US 2003-446230P	P 20030210

AB Compns. comprise the tannates of opioids. The opioid tannate may be readily prepared by reacting an opioid free base such as hydrocodone or oxycodone with tannic acid, either neat or in the presence of up to about 30 weight % water, at a temperature of about 60 to about 150° C. and thereafter recovering the resultant opioid tannate. The opioid tannate may also be prepared by an alternative process that involves reacting the opioid free base with water at a temperature such that not more than about 10
weight % of the opioid tannate will be decomposed and thereafter removing the
water by freeze-drying.
IT **79413-55-1DP**, tannate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opioid tannate compns.)
RN 79413-55-1 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-methyl-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

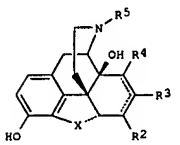
L4 ANSWER 2 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:174339 CA
TITLE: The first example of the stereoselective synthesis of 7β-carbamoyl-4,5α-epoxymorphinan via a novel and reactive γ-lactone
AUTHOR(S): Fujii, Hideaki; Hirano, Noriyuki; Uchiro, Hiromi; Kawamura, Kuniaki; Nagase, Hiroshi
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Toray Industries, Inc., Kamakura, 248-8555, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2004), 52(6), 747-750
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:174339
AB 7β-Carbamoyl-4,5α-epoxymorphinans were stereoselectively synthesized from the 7α-carboxylate intermediate in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and amines under reflux conditions in mesitylene via a novel and reactive 7β,14β-γ-lactone. These were the first examples of the stereoselective syntheses of 7β-substituted 4,5α-epoxymorphinans. The mechanism of the reaction process was elucidated as follows: (1) epimerization of 7α-carboxylate, (2) intramol. lactonization of 7β-carboxylate, and (3) aminolysis of the resultant γ-lactone. The aminolysis of the isolated reactive γ-lactone with allylamine and the alcoholysis with MeOH in the presence of NaBH4 proceeded at room temperature The γ-lactone can be a useful intermediate for the preparation of 7β-substituted 4,5α-epoxymorphinans that would be potent selective δ opioid receptor ligands. The stereoselective syntheses of the 7α-carbamoyl-4,5α-epoxymorphinans from 7α-carboxylate via 7α-carboxylic acid were also successful.
IT **735332-86-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and δ-opioid receptor antagonistic activity of)
RN 735332-86-2 CA
CN Morphinan-7-carboxamide, 17-(cyclopropylmethyl)-4,5-epoxy-3,6,14-trihydroxy-N-(2-propenyl)-, (5α,6α,7β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

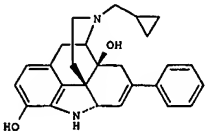
L4 ANSWER 3 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:309366 CA
TITLE: Opiate analogs selective for the δ-opioid receptor
INVENTOR(S): Welsh, William J.; Yu, Seong Jae; Nair, Anil
PATENT ASSIGNEE(S): The Curators of the University of Missouri, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026819	A2	20040401	WO 2003-US29455	20030918
WO 2004026819	A3	20040701		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498046	AA	20040401	CA 2003-2498046	20030918
US 2004122230	A1	20040624	US 2003-665377	20030918
EP 1539767	A2	20050615	EP 2003-756835	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			US 2002-411724P	P 20020918
			WO 2003-US29455	W 20030918

OTHER SOURCE(S): MARPAT 140:309366
GI



I

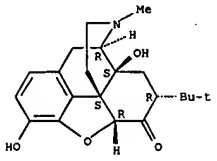


II

AB Novel compds., such as I [X = O, S, NH, etc.; R2 = H, oxo, CMe3, OPh, NPh2, SPh, cyclohexyl; R3 = Ph, OPh; R2R3 = fused carbocycle or heterocycle; R4 = H, CMe3; R3R4 = fused carbocycle or heterocycle; R5 = Me, cyclopropylmethyl; alkyl; R6 = H, Me, alkyl], which were predicted by 3D-QSAR models to selectively bind to the δ-opioid receptor, were designed for use in pharmaceutical compns. for the treatment of immune disorders, transplant rejection, allergy, inflammation, drug or alc.

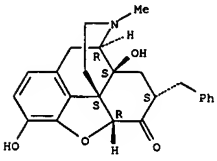
L4 ANSWER 3 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)
abuse, diarrhea, cardiovascular disease, respiratory disease and pain and for protecting brain cells and decreasing gastric secretion. These compds. have greater selectivity, improved water (blood) soly., and enhanced therapeutic value as analgesics. E.g., opioid II gave a calcd. logP value of 3.2 vs 2.65 for naltrindole. General synthetic schemes for the prepn. of these opioids were discussed. Because agonists with selectivity for the δ-opioid receptor have shown promise in providing enhanced analgesis without the addictive properties, the compds.
of the present invention are better than morphine, naltrindole, spiro[indanyloxymorphone], and other known μ-opioid receptor selectors as analgesics.
IT 676227-53-5P
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opiate analogs selective for the δ-opioid receptor)
RN 676227-53-5 CA
CN Morphinan-6-one, 7-(1,1-dimethylethyl)-4,5-epoxy-3,14-dihydroxy-17-methyl-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)
demonstrated in rats.
IT 471281-05-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 7-substituted morphinan derivs. as remedies for frequent urination and urinary incontinence)
RN 471281-05-7 CA
CN Morphinan-6-one, 4,5-epoxy-3,14-dihydroxy-17-methyl-7-(phenylmethyl)-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



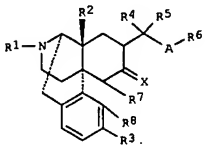
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:311074 CA
TITLE: Preparation of 7-substituted morphinan derivatives as remedies for frequent urination and urinary incontinence
INVENTOR(S): Kawamura, Kuniaki; Tanaka, Toshiaki; Fujimura, Morihiro; Komagata, Toshikazu; Hasebe, Ko; Ito, Hiroaki
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002081477	A1	20021017	WO 2002-JP3054	20020328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: JP 2001-102726 A 20010330

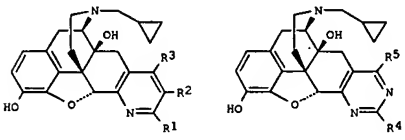
OTHER SOURCE(S): MARPAT 137:311074
GI



I

AB The title compds. I [A = (CH2)n; n = 0 - 5; R1 = H, alkyl, etc.; R2 = H, OH, etc.; R3 = H, OH, etc.; R4 = H, alkyl, etc.; R5 = H, alkyl; or R4R5 = oxo; R6 = (un)substituted organic moiety (e.g., Ph, etc.); R7 = H; R8 = OH, alkoxy; or R7R8 = O; X = O, etc.] are prepared The effect of compds. of this invention at 0.3 mg/kg on urinary bladder contraction was

L4 ANSWER 5 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:322799 CA
TITLE: Synthesis, Opioid Receptor Binding, and Biological Activities of Naltrexone-Derived Pyrido- and Pyrimidomorphinans
AUTHOR(S): Ananthan, Subramaniam; Kezar, Hollis S., III; Carter, Ronald L.; Saini, Surendra K.; Rice, Kenner C.; Wells, Jennifer L.; Davis, Peg; Xu, Heng; Dersch, Christina M.; Bilsky, Edward J.; Porreca, Frank; Rothman, Richard B.
CORPORATE SOURCE: Organic Chemistry Department, Southern Research Institute, Birmingham, AL, 35255, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(18), 3527-3538
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II

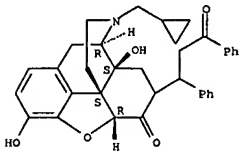
AB A series of pyrido- and pyrimidomorphinans, e. g. I (R1 - R3 = H; R1 = Ph, R2 = R3 = H; R1 = R3 = H, R2 = Ph; R1 = R3 = H, R2 = C6H4Cl-4; R1 = H, Me, Ph, R2 = H, R3 = Ph; R1R2 = CH:CHCH:CH, R3 = Ph) and II (R4 = R5 = H; R4 = Me, Ph, R5 = H; R4 = H, Me, CH2Ph, Ph, R5 = Ph), resp., were synthesized from naltrexone and evaluated for binding and biol. activity at the opioid receptors. The unsubstituted pyridine I (R1 - R3 = H) displayed high affinities at opioid δ, μ, and κ receptors with Ki values of 0.78, 1.5, and 8.8 nM, resp. Compound I (R1 - R3 = H) was devoid of agonist activity in the mouse vas deferens (MVD) and guinea pig ileum (GPI) prepns. but was found to display moderate to weak antagonist activity in the MVD and GPI with Ke values of 37 and 164 nM, resp. The pyrimidomorphinans in general displayed lower binding potencies and δ receptor binding selectivities than their pyridine counterparts. Incorporation of aryl groups as putative δ address mimics on the pyrido- and pyrimidomorphinan framework gave ligands with significant differences in binding affinity and intrinsic activity. Attachment of a Ph group at the 4'-position of I (R1 - R3 = H) or the equivalent 6'-position of II (R4 = R5 = H) led to dramatic reduction in binding potencies at all the

L4 ANSWER 5 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)
three opioid receptors, indicating the existence of a somewhat similar steric constraint at the ligand binding sites of δ, μ, and κ receptors. In contrast, the introduction of a Ph group at the 5'-position of I (R1 - R3 = H) did not cause any redn. in the binding affinity at the δ receptor. In comparison to the unsubstituted pyridine I (R1 - R3 = H), the 5'-phenylpyridine I (R1 = R3 = H, R2 = Ph) showed improvements in μ/δ and κ/δ binding selectivity ratios as well as in the δ antagonist potency in the MVD. Interestingly, introduction of a chlorine atom at the para position of the pendant 5'-Ph group of I (R1 = R3 = H, R2 = Ph) not only provided further improvements in δ antagonist potency in the MVD but also shifted the intrinsic activity profile of I (R1 = R3 = H, R2 = Ph) from an antagonist to that of a μ agonist in the GPI. Compd. I (R1 = R3 = H, R2 = C6H4Cl-4) thus possesses the characteristics of a nonpeptide μ agonist/δ antagonist ligand with high affinity at the δ receptor (Ki = 2.2 nM), high antagonist potency in the MVD (Ke = 0.66 nM), and moderate agonist potency in the GPI (IC50 = 163 nM). Antinociceptive evaluations in mice showed that intracerebroventricular (icv) injections of I (R1 = R3 = H, R2 = C6H4Cl-4) produced a partial agonist effect in the 55 °C tail-flick assay and a full agonist effect in the acetic acid writhing assay (A50 = 7.5 nmol). No signs of overt toxicity were obsd. with this compd. in the dose ranges tested. Moreover, repeated icv injections of an A90 dose did not induce any significant development of antinociceptive tolerance in the acetic acid writhing assay. The potent δ antagonist component of this mixed μ agonist/δ antagonist may be responsible for the diminished propensity to produce tolerance that this compd. displays.

IT **248273-52-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, opioid receptor binding, and biol. activities of naltrexone-derived pyrido- and pyrimidomorphinans)

RN 248273-52-1 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-(3-oxo-1,3-diphenylpropyl)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 5 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CA COPYRIGHT 2005 ACS on STN

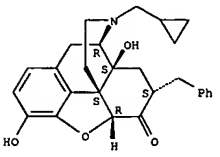
ACCESSION NUMBER: 130:231893 CA
TITLE: A uniform molecular model of δ opioid agonist and antagonist pharmacophore conformations
AUTHOR(S): Brandt, Wolfgang
CORPORATE SOURCE: Institute of Biochemistry, Martin-Luther-University Halle-Wittenberg, Halle, D-06099, Germany
SOURCE: Journal of Computer-Aided Molecular Design (1998), 12(6), 615-621
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB On the basis of a model of the pharmacophore conformations of agonist of the δ-opioid receptor the corresponding δ-antagonist conformations were determined by means of force field calcns. The results explain the unusual behavior of several cyclic β-casomorphin analogs on the mol. level. Thus, for instance, the model helps to understand why Tyr-c[D-Orn-2-Nal-D-Pro-Gly] is a mixed μ-agonist and δ-antagonist. Furthermore, the model is consistent with low energy conformations of other δ-antagonists such as Tyr-Tic-Phe, Tyr-Tic-Phe-Phe, naltrindole and BNTX. The occupation of a special spatial area by bulky groups close to the protonated N-terminus of opioid peptides is assumed to be highly critical for the switch from agonist to antagonist behavior.

IT **153567-06-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(uniform mol. model of δ-opioid agonist and antagonist pharmacophore conformations)

RN 153567-06-7 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-(phenylmethyl)-, (5α,7α)- (9CI) (CA INDEX NAME)

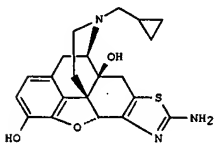
Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 127:307524 CA
TITLE: Synthesis of 2'-amino-17-cyclopropylmethyl-6,7-dehydro-3,14-dihydroxy-4,5α-epoxy-6,7:4',5'-thiazolomorphinan from naltrexone
AUTHOR(S): Nan, Yang; Xu, Wei; Zaw, Kyaw; Hughes, Kathrine E.; Huang, Liang-Fu; Dunn, William J., III; Bauer, Ludwig; Bhargava, Hemendra N.
CORPORATE SOURCE: College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612-7231, USA
SOURCE: Journal of Heterocyclic Chemistry (1997), 34(4), 1195-1203
CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:307524
GI



I

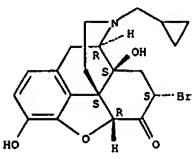
AB Fusion of an azole moiety at C-6 and C-7 of naltrexone was illustrated by the synthesis of thiazolomorphinan I. Bromination of 3-O-methylnaltrexone led to the 1,7α-dibromo derivative which reacted with thiourea to attach the 2-aminothiazole ring to C-6 and C-7 of naltrexone. After converting the amino and alc. groups to trimethylsilyl derivs., the aromatic bromo group was removed by halo-lithium inter-change with butyllithium, followed by hydrolysis with water. In the final step of the synthesis, the Me ether was cleaved by boron tribromide to generate I. An alternate synthesis of I commenced with 3-O-acetylnaltrexone (II). Bromination of II in acetic acid in the presence of hydrobromic acid produced a mixture of 3-O-acetyl-7α-bromonaltrexone and 7α-bromonaltrexone, both, as hydrobromides. Reaction of this mixture of hydrobromides with thiourea furnished I in 62% overall yield. While 1H and 13C chemical shifts of all compds. have reported, those of 7α-bromonaltrexone hydrobromide and I.2HCl were established unequivocally.

IT **197242-22-1P**, 7α-Bromonaltrexone hydrobromide
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2'-amino-17-cyclopropylmethyl-6,7-dehydro-3,14-dihydroxy-4,5α-epoxy-6,7:4',5'-thiazolomorphinan from naltrexone)

RN 197242-22-1 CA
CN Morphinan-6-one, 7-bromo-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-,

L4 ANSWER 7 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)
hydrobromide, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HBr

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

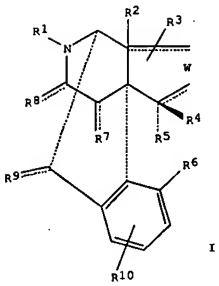
L4 ANSWER 8 OF 10 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	123:9747 CA
TITLE:	Preparation of morphinan derivatives as brain cell protecting agents
INVENTOR(S):	Nagase, Hiroshi; Hayakawa, Jun; Kawamura, Huniaki; Kawai, Koji; Endoh, Takashi
PATENT ASSIGNEE(S):	Toray Industries, Inc., Japan
SOURCE:	PCT Int. Appl., 455 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9503308	A1	19950202	WO 1994-JP1197	19940720
W: AU, CA, JP, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2143864	AA	19950202	CA 1994-2143864	19940720
AU 9472373	A1	19950220	AU 1994-72373	19940720
AU 686203	B2	19980205		
EP 663401	A1	19950719	EP 1994-921794	19940720
EP 663401	B1	20000607		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ES 2146654	T3	20000816	ES 1994-921794	19940720
US 6177438	B1	20010123	US 1996-754750	19961121
PRIORITY APPLN. INFO.:			JP 1993-202127 A	19930723
			WO 1994-JP1197 W	19940720
			US 1994-279030 B1	19940722

OTHER SOURCE(S): MARPAT 123:9747
GI

L4 ANSWER 8 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)



I

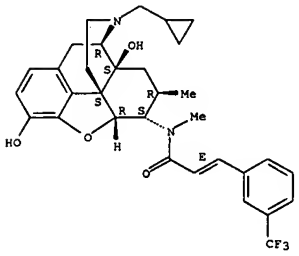
AB Morphinan derivs. I [R1 = alkyl, cycloalkylalkyl, etc.; R2 = -A-B-R11; A = bond, CO, XC(:Y)-, XC(:Y)Z-, etc.; B = bond, alkylene, etc.; X, Y, Z = (un)substituted imino, S, O; R11 = H, NO2, F, Cl, etc.; R3 (may be more than one substituent) = A-B-R11; R4 = A-B-R11; R5, R6 = H, OH, F, Cl, Br, etc.; R7 = H, OH, F, Cl, Br, iodo, etc.; R8 = H, alkyl, cyano, CO2H, alkylamide, carbonyl; R9 = H, OH, F, Cl, Br, iodo, etc.; R10 (may be more than one substituent) = H, OH, F, Cl, Br, iodo, SO3H, etc.; W = alkylene, hydrocarbyl] or their pharmacol. acceptable acid-addition salts, useful as brain cell protecting agents, are prepared These compds. have potent analgesic, diuretic and antitussive effects as highly selective κ-opioid agonists, and are useful as analgesic, diuretic and antitussive agents. In addition, they have a significant brain cell protective effect and are useful as a brain cell protective agent. Thus, naltrexone was reacted with methylamine hydrochloride in MeOH at room temperature for 20 min followed by hydrogenation in the presence of platinum oxide to give 17-cyclopropylmethyl-4,5-epoxy-3,14β-dihydroxy-6α-methylaminomorphinan isolated as the hydrochloride salt. This had an ED50 of 0.017 mg/Kg in an acetic acid writhing analgesic experiment

IT **163713-18-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of morphinan derivs. as brain cell protecting agents)

RN 163713-18-6 CA
CN 2-Propenamide, N-[(5α,6α,7β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-methylmorphinan-6-yl]-N-methyl-3-[3-(trifluoromethyl)phenyl]-, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 8 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)



● HCl

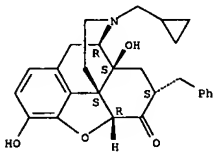
L4 ANSWER 9 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 120:182343 CA
TITLE: Synthesis of naltrexone-derived δ-opioid antagonists. Role of conformation of the δ address moiety
AUTHOR(S): Portoghese, P. S.; Sultana, M.; Moe, S. T.; Takemori, A. E.
CORPORATE SOURCE: College of Pharmacy, University of Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(5), 579-85
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Naltrindole (NTI) is a highly potent and selective δ-opioid receptor antagonist. In an effort to understand the origin of the high potency, affinity, and selectivity of NTI, the authors have examined the conformational role of its indolic benzene moiety through the synthesis of related naltrexone derivs. which contain the benzene moiety in different orientations and at different attachments in the mol. One of these naltrexone derivs., whose 7-indanyl benzene moiety is orthogonal to ring C of the morphinan system, is a potent δ-opioid receptor antagonist in vitro and in vivo. Computer-assisted mol. overlay studies of the minimized structures revealed the importance of the position of the benzene moiety for effective interaction with δ-opioid receptors. In several compds., the aromatic ring falls in the same region of space as that of the indolic benzene moiety of NTI, and all of these ligands possessed significant activity at δ-opioid receptors. Analogs which were shown to have relatively weak δ-opioid receptor antagonist potency have their aromatic groups located in a space that is different from that of the more potent analogs.

IT **153567-06-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and δ-opioid antagonism by, structure in relation to)

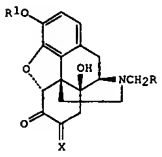
RN 153567-06-7 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-(phenylmethyl)-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 9 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)

L4 ANSWER 10 OF 10 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 95:180662 CA
TITLE: Analgesic narcotic antagonists. 8. 7α-Alkyl-4,5α-epoxymorphinan-6-ones
AUTHOR(S): Kotick, Michael P.; Leland, David L.; Polazzi, Joseph O.; Howes, John F.; Bousquet, Ann R.
CORPORATE SOURCE: Chem. Dep., Miles Lab. Inc., Elkhart, IN, 46515, USA
SOURCE: Journal of Medicinal Chemistry (1981), 24(12), 1445-50
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

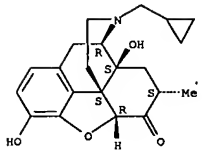
AB Thirty-six title compds., most of the structure I (R = H, cyclopropyl, cyclobutyl; R1 = H or Me; X = CHNMe2, ZH, H and Me, etc.) were synthesized and tested in mice for antinociceptive and narcotic antagonist activities. I (R = H, X = H and α-Me) were almost as potent antinociceptives as dihydrocodeinone. I with larger alkyl groups at position 7 were less potent. Corresponding I (R = cycloalkyl) did not have strong mixed agonist-narcotic antagonist activities.

IT **79413-55-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and analgesic and narcotic antagonist activities of, structure in relation to)

RN 79413-55-1 CA
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy-7-methyl-, (5α,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 10 OF 10 CA COPYRIGHT 2005 ACS on STN (Continued)



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L2            4 S L1 SAM
L3           77 S L1 FULL

     FILE 'CA' ENTERED AT 09:28:55 ON 30 SEP 2005
L4           10 S L3

=>

---Logging off of STN---


=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    58.00     219.54

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -8.16      -8.16

STN INTERNATIONAL LOGOFF AT 09:30:25 ON 30 SEP 2005
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